Section: FMHS

Original Research Article

PREVALENCE OF SUBCLINICAL HYPOTHYROIDISM IN METABOLIC SYNDROME AND CORRELATION WITH ITS COMPONENTS

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ABSTRACT

Background: Several studies worldwide have studied the correlation between subclinical hypothyroidism (SCH), and metabolic syndrome (MetS), but have reported inconsistent findings. **Objectives:** To assess the correlation between SCH and MetS in a population.

Materials & Methods: This cross-sectional study was conducted at the SGT hospital, Gurugram and analyzed all thyroid function tests conducted between January 2019, to December 31, 2021. A predesigned checklist was used to collect data about patients' characteristics such as age, gender, nationality, TSH, FT4 level, and MetS components.

Results: The study was performed at the department of Medicine in the SGT medical college, hospital& research institute, Budhera, Gurgaon, Haryana, India during December 2018 to May 2020. 150 subjects were included in the study – 100 patients of metabolic syndrome and 50 healthy controls. Data was retrieved and analysed. The observations are presented under 4 sections.

Conclusion: The study demonstrated that the prevalence of SCH is similar between both genders but increases with age. MetS components were abnormal in patients aged >50 years and in males with SCH. SCH and MetS components were found to be correlated, and thus monitoring these variables in patients with SCH is advisable.

Keywords: Body mass index, cardiovascular risk factors, diabetes, dyslipidemia, hypertension, metabolic syndrome, obesity, subclinical hypothyroidism.

INTRODUCTION

The "deadly quartet" constitutes of hypertension, high triglyceride levels, low high- density lipoproteins and abnormal fasting glucose levels in obese individuals. It is also refereed as a "metabolic syndrome (MetS) " and "syndrome X",[1,2] In this syndrome, mortality risk is getting doubleted due to myocardial infarction and other cardiovascular risk factors. They have three times more risk to have stroke as compared to normal population,[3] Insulin resistance is identified as the central pathophysiological phenomenon underlying this syndrome.[4] Obesity, sedentary lifestyle, aging, dyslipidaemia, cardiovascular disease, lipodystrophy etc are some of the risk factors for developing metabolic syndrome.

The correlation between Subclinical Hypothyroidism and MetS has not been extensively investigated in prospective controlled studies and only a few studies are available in the world literature. Besides there being a paucity of any further research on this subject in India, few studies have been done on North Indian Patients. Therefore, a study based on the prevalence of subclinical hypothyroidism in patients with MetS and its relation with the components of MetS holds importance and as per our knowledge no such type of study has been done earlier in this institution.

MATERIAL AND METHODS

The Cross sectional study- a single centre observational study was conducted in the medical

outpatient departments and medical wards at the SGT hospital, Gurugram on
100 patients and 50 controls of the age group of 20 to 75 years who fulfilled the inclusion criteria and gave written informed consent for the study after due deliberation over duration of 18 months after ethical clearance from the institute ethics committee

Inclusion criteria

Patients with Metabolic Syndrome who fulfilled the Modified NCEP-ATP III (National
Cholesterol Education Program Expert Program and Adult Treatment Panel III) criteria for Asians proposed by AHA [American Heart Association] (3 out of 5 criteria positive) were included in the study;

1. Blood Pressure > or =130/85 mmHg or on antihypertensive medications.
2. Fasting plasma glucose > or =100mg/dl or on anti-diabetic medications.
3. Fasting triglycerides > or =150mg/dl or under treatment.
4. HDL cholesterol <40 mg/dl in males and <50 mg/dl in females or under treatment,
5. Abdominal Obesity (Waist circumference): > or = 90 cm in South Asian men and > or = 80 cm in South Asian women will be included in the study group.

Exclusion criteria

The following patients were excluded from the study.

1. Patients with known case of hypothyroidism and under treatment for any thyroid related disorders.
2. Renal disorders and liver disorders
3. Congestive Cardiac failure
4. Pregnant women
5. Patients who are taking on oral contraceptive pills, statins and other medications that can alter thyroid functions (e.g. lithium, amiodarone or interferon gamma) would be excluded from the study.
6. Patients <20 years and > 75 years of age will not be considered.
7. Acutely ill patients as they have sick euthyroid syndrome.

Methodology

1. Detailed history, symptoms, signs, history of any previous medication and anthropometric measurements like waist circumference of all the subjects was noted in a patient information sheet/proforma.
2. Past, Family and Personal history of all the patients were asked in detail regarding Hypertension, type 2 Diabetes Mellitus, Ischemic Heart Disease, Dyslipidemia and Thyroid dysfunction, Smoking and Alcohol.
3. All candidates will be explained about the purpose and nature of the study.
4. Written and informed consent was taken.
5. 100 patients who fulfilled the criteria [3 out of 5 criteria presents] of metabolic syndrome were included in the study group.
6. In the control group, 50 patients with no features of metabolic syndrome [0 out of 5 criteria] were included.
7. Baseline data collection and a detailed physical examination for both the study and control group were performed.

The data was compiled and analysed using MS Excel (R) office 365, GraphPad prism 8.4.2 and SPSS version 25 with P value of <0.05 considered significant.

RESULTS

The study was performed at the department of Medicine in the SGT medical college, hospital& research institute, Budhera, Gurgaon, Haryana, India during December 2018 to May 2020. 150 subjects were included in the study – 100 patients of metabolic syndrome and 50 healthy controls. Data was retrieved and analysed. The observations are presented under 4 sections.

Section 1. Observations for metabolic syndrome patients (cases) versus Healthy controls

Section 2. Observations of thyroid function tests in Metabolic syndrome Vs Healthy controls.

Section 3. Observations for Subclinical Hypothyroidism in Metabolic syndrome Vs Healthy controls.

Section 4. Corelation of various components of MetS with Subclinical Hypothyroidism.

Section 1. Observations for metabolic syndrome patients (cases) versus Healthy controls

Age wise comparison

The average age of patients with metabolic syndrome was higher than the controls (50.57 vs 42.64 years). The difference was statistically significant (P-0.0007).

The proportion of patients with age 40 years of more in patients with metabolic syndrome (78, 78%) was significantly higher than that in patients who were healthy controls (29, 58%).

Gender wise distribution comparison

The proportion of males and females in both the groups was similar with no statistically significant difference (P – 0.3355).

Systolic BP related parameter comparison.

Patients with metabolic syndrome had a higher systolic BP on average (138.20 mm Hg) compared to controls (122.04 mm Hg). The difference was statistically significant (P
<0.0001).

Systolic BP distribution comparison

The proportion of patients with systolic BP 130 mm Hg or more in patients with metabolic syndrome (92, 92%) was significantly higher than the proportion in healthy controls (2, 4%). [Table 1]

Patients with metabolic syndrome had a higher diastolic BP on average (89.36 mm Hg) compared to controls (82.22 mm Hg). The difference was statistically significant (P
<0.0001).

Diastolic BP distribution comparison

The proportion of patients with Diastolic BP 85 mm Hg or more in patients with metabolic syndrome (90, 90%) was significantly higher than the proportion in healthy controls (12, 24%).

The results were significant statistically (<0.0001).

FBS related parameter comparison

The fasting blood sugar levels were higher for the patients with metabolic syndrome (152.743 mg/dl) compared to 88.90 mg/dl in the healthy controls. The difference was statistically significant (P<0.0001).

FBS distribution comparison

The proportion of patients with FBS 100 mg/dl or more (84, 84%) was significantly higher than that in the healthy controls (0,0%).

HDL related parameter comparison

The average HDL levels in patients with metabolic syndrome (40.33 mg/dl) was significantly lower (P<0.0001) compared to the healthy controls (53.33 mg/dl).

HDL distribution comparison

The proportion of patients with HDL levels below the prescribed limits for either gender was more in the patients with metabolic syndrome (68, 68%) compared to the healthy controls (1, 2%).

Triglycerides related parameter comparison

The average triglyceride levels were significantly higher in patients with metabolic syndrome compared to the healthy controls (212.311 vs 105.18, P<0.0001).

Triglycerides based distribution comparison

The proportion of patients with triglyceride levels 150 mg/dl or more than 150 mg/dl was more in the patients with metabolic syndrome (64, 64%) compared to the healthy controls (0, 0%).

Waist circumference related parameter comparison

The average waist circumference was significantly higher (P<0.0001) in the patients with metabolic syndrome (89.25 cms) compared to healthy controls (78.24 cms).

Waist circumference-based distribution comparison

The proportion of patients with waist circumference above the prescribed limits was significantly higher in the patients with metabolic syndrome (91, 91%) compared to healthy controls (0, 0%).

Clinical history-based comparison

Proportion of patients with hypertension in the group with metabolic syndrome (96, 96%) was significantly higher compared to healthy controls (49, 98%)

The proportion of patients with waist circumference above the prescribed limits was significantly higher in the patients with metabolic syndrome (91, 91%) compared to healthy controls (0, 0%).

History of Diabetes /oral hypoglycemic medication.

Proportion of patients with diabetes in the group with metabolic syndrome (96, 96%) was significantly higher compared to healthy controls (50, 100%).

History of hypolipidemic drugs

Proportion of patients with hypolipidemic drug use in the group with metabolic syndrome (41, 41%) was significantly higher compared to healthy controls (0,0%).

Section 2. Observations of thyroid function tests in Metabolic Syndrome Vs Healthy controls.

Thyroid profile-based comparison

TSH related parameters comparison

The average TSH level in patients with metabolic syndrome (3.41 mIU/ml) was higher than in the healthy controls (2.94 mIU/ml). The difference was not statistically significant (P=0.7139).

Free T3 related parameters comparison

The free T3 levels were lower in patients with metabolic syndrome compared to the healthy controls (2.97 vs 3.31 ng/dl). The difference was not statistically significant (P=0.1751).

Free T4 related parameters comparison

The free T4 levels were higher in patients with metabolic syndrome compared to the healthy controls (2.03 vs 1.55 ng/dl). The difference was not statistically significant (P=0.1751).

Section 3. Observation for Subclinical Hypothyroidism in Metabolic syndrome patients Vs Healthy controls.

Subclinical hypothyroidism related distribution comparison

The proportion of patients with metabolic syndrome having subclinical hypothyroidism was higher (19, 19%) compared to the healthy controls (8, 16%). The difference in proportion was not statistically significant (P=0.6532).

Section 4. Correlation of various components of Metabolic Syndrome with Subclinical Hypothyroidism.

Age wise comparison

Age related parameter comparison

The average age of metabolic syndrome patients with subclinical hypothyroidism (50.31 years) was similar to the patients without subclinical hypothyroidism (50.62 years). The results were comparable with no significant difference statistically (P=0.9669).

Age wise distribution comparison

The distribution of metabolic syndrome patients based on subclinical hypothyroidism status was comparable/not significantly different.

Gender wise distribution

Gender wise distribution comparison

Amongst the patients with metabolic syndrome, the proportion of females in patients with subclinical hypothyroidism (15, 78.94%) was significantly higher (P<0.0001) than that of females in patients with no subclinical hypothyroidism (47, 58.02%).

Table 1: Systolic BP related parameter comparison

Mann Whitney test	
P value	<0.0001
Exact or approximate P value?	Exact
P value summary	****
Significantly different (P < 0.05)?	Yes
One- or two-tailed P value?	Two-tailed
Sum of ranks in column F, AG	9746, 1579
Mann-Whitney U	304

Table 2: Univariate analysis for Subclinical hypothyroidism prevalence

Parameter		Subclinical hypothyroidism present	Subclinical hypothyroidismabsent	P value
Age in years	<40 years	6 (31.58)	16 (19.75)	0.2651
	40-60 years	6 (31.58)	38 (46.91)	0.2279
	60 and above	7 (36.84)	27 (33.33)	0.6027
Gender	Males	4 (21.05)	34 (41.98)	
	Females	15 (78.95)	47 (58.02)	<0.0001
Systolic blood pressure (in mmhg)	Less than 130	2 (10.52)	6 (7.40)	
	130 or more	17 (89.47)	75 (92.59)	0.6534
Diastolic blood pressure (in mmhg)	Less than 85	1 (5.26)	9 (11.11)	
	85 and above	18 (94.73)	72 (88.89)	0.4465
Fasting bloodsugar (mg/dl)	Less than 100	3 (15.78)	13 (16.04)	
	100 or more	16 (84.21)	68 (83.95)	0.8022
HDL	<40/<50	14 (73.68)	54 (66.67)	
	40 or more/50 ormore	5 (26.31)	27 (33.33)	0.5575
Triglyceride	Less than 150mg/dl	5 (26.31)	31 (38.27)	
	150 or more	14 (73.68)	50 (61.72)	0.3308
Waist circumference	<80/<90	1 (5.26)	8 (9.87)	
	80 and above/ 90	18 (94.73)	73 (90.12)	0.5294
	and above			
HTN	No	2 (10.52)	2 (2.46)	
	Yes	17 (89.47)	79 (97.53)	0.108
Diabetes	No	2 (10.52)	2 (2.46)	
	Yes	17 (89.47)	79 (97.53)	0.108
Hypolipidemicdrugs	No	9 (47.36)	50 (61.72)	
	Yes	10 (52.63)	31 (38.27)	0.254

Table 3: Multivariate analysis of Predictors and risk factors for subclinical hypothyroidism

Parameter	B covariate	Exp B (Oddsratios)	P value Significance
Age more than 60 years	0.154	1.167	0.772
Gender - Male (Reference – Females)	-0.998	0.369	0.100
Systolic BP more than 130 mm Hg	-0.26	0.771	0.766
Diastolic BP more than 85 mm Hg	0.982	2.67	0.372
ystolic BP more than 130 mm Hg andDiastolic BP more than 85 mm Hg	0.245	1.227	0.771
Fasting blood sugar greater than 100	-0.089	0.915	0.909
vated HDL levels (beyond acceptedgender wise limits)	-0.22	0.802	0.706
evated Triglyceride levels (more than150)	0.455	1.577	0.433
st circumference elevated (beyondaccepted gender wise limits)	0.172	1.188	0.884
Pre-existing hypertension	-1.222	0.2985	0.275
Pre-existing Diabetes	-1.222	0.2985	0.275
Pre-existing Hypolipidemic drugs	0.609	1.839	0.244

DISCUSSION

Out of a total of 150 subjects enrolled, 100 patients were of metabolic syndrome and 50 were healthy controls. Out of these 100 patients were of metabolic syndrome, 19 were with Subclinical hypothyroidism and 81 patients were with no Subclinical hypothyroidism. This finding is in accordance to studies done by Uzunlulu M and Shrestha S.5 Sub clinical hypothyroidism prevalence in our study was found to be 19%. TFT was done in all patients so estimated higher prevalence could be due to the same.

The mean age of presentation was 50.31 ± 13.63 years in patients of metabolic syndrome patients with subclinical hypothyroidism. The maximum numbers of patients were in the age group of 60 years and above and were females in both the groups (78.95% & 58.02). The proportion of females in patients with subclinical hypothyroidism was significantly higher which is in concordance with a study conducted by Shantha GP et al where females were predominant as compared to males.6 Also, a study by Sorkhou EI et al showed 28% prevalence in 40-55-year-old followed 57.8% in above 55-year-old patients.[7]

The average waist circumference was significantly higher in the patients with metabolic syndrome (89.25 cms) compared to healthy controls (78.24 cms). Waist circumference is most common component in male and female both. The high prevalence can be due to low cut off for waist circumference for Asian population (>80 cm female,>90 cm in male for Asian population instead of >102 cm in male and >88cm for female). Second most component is low HDL in both the sex. Third most component in male is high FBS and in female it is high triglyceride. This distribution is comparable to a study done by Yasein N et al.[8]

The patients with subclinical hypothyroidism had lower levels of HDL compared to the other group (38.15 vs 40.84 mg/dl). Moreover, patients with subclinical hypothyroidism had higher levels of mean TG levels (258 vs 201.54 mg/dl). The mean waist circumference was slightly higher in the patients with subclinical hypothyroidism group (90.26 vs 89.01 cms).

Proportion of patients with subclinical hypothyroidism having a history of hypolipidemic drug use was much higher (52.63%) than that in patients without subclinical hypothyroidism (38.27%). It is well known and proven that, by treating with levothyroxine replacement in all overt or clinical hypothyroid patients, we can reduce all the metabolic parameters and cardiovascular risk.[9]

Predictors/Risk factors for subclinical hypothyroidism in metabolic syndrome patients were analyzed in our study and showed that MetS patients with age >60 years; female gender; diastolic BP >85 mm Hg; patients with both high Systolic BP (>135 mmHg) & Diastolic BP (>85 mm Hg); lower levels of HDL; elevated triglyceride levels; high waist circumference; history of pre-existing hypolipidemic medications are associated with elevated odds of having subclinical hypothyroidism.

On the univariate analysis of all the parameters only female gender had a positive correlation with presence of the subclinical hypothyroidism (p value < 0.0001) while other factors like age, blood pressure, fasting blood sugar, HDL, TG, waist circumference, HTN, Diabetes, hypolipidemic drugs had no statistically significant correlation .

While on multivariate analysis of all the risk factors none of them had a statistically significant relation of presence of subclinical hypothyroidism among the cases studied.

Furthermore, predictors or risk factors for subclinical hypothyroidism if present in patients of MetS, will certainly increase the chances of getting subclinical hypothyroidism. So it is always prudent to look for thyroid dysfunction to achieve optimal outcome while managing MetS patients.

CONCLUSION

This study clearly indicates and emphasizes a diehard need for investigating the presence of thyroid dysfunction while managing patients with MetS.

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